September 21, 1953

Dr. P. Armitage
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Dear Dr. Armitage:

I was most pleased to note your article on the statistical theory of
bacterial mutation in the last Journal of Hygiene. The discussion at this
level should be of considerable value to workers dealing with this problem.
But perhaps the most impressive conclusion is how unsatisfactory are the
estimates determined from counts of mutants. I think there is little doubt
that the technique used by Novick and Szilard (as cited by yourself, and
in the Cold Spring Harbor Symposium, 1951) is by far the best approach to
the measurement of rates.

In teaching this subject to a class with very poor mathematical prepara-
tion, I have found it expedient to focus on the "mean clone size", i.e.,
$y/m = my$ $r/aN = d$, and to explain the effects of phenotypic delay, dominance,
and assumptions on the mutational model as they influence d. If I interpret
you correctly, we are agreed that the least ambiguous unit for expressing
rates is the probability of mutation per bacterial division. Many bacterialo-
gists with a rudimentary training in the calculus have had great difficulty
with the unit "per bacterium per division". If we can someday find a system
in which phenotypic delay can be discounted, it would be worthwhile to test
the mutation models by direct estimation of d, e.g. from a Newcombe's type
of experiment.

The enclosed sheet may be of doubtful interest to you.

From other lines of work it is possible to get some assurances on the
matter of dominance. Almost all of the mutations that have been exploited
for rate measurements are recessive, e.g., resistance to bacteriophages,
resistance to drugs, requirement for growth factors. However, the "reversions'
to nutrilite independence (e.g. histidineless to wild type), and from lactose-
negative to lactose-positive, are almost certainly dominant. However, too
little is known of phenotypic delay and, correlatively, of the extent to which
the existing phenotypes of the cells are tested (rather than that of their des-
cendants) to draw a full picture of any of these systems.

If not too much of the imposition, may I enter a request for an additional
to you for a past favor and will reciprocate with any of our papers on subjects

of mutual interest.